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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,323	12/19/2005	David Gershon	JG-RP-5170PCT/US/500561.2	5879

28062 7590 03/29/2010

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EXAMINER	
ZAREK, PAUL E	
ART UNIT	**PAPER NUMBER**
1628	
MAIL DATE	**DELIVERY MODE**
03/29/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/561,323	GERSHON, DAVID	
	Examiner	Art Unit	
	Paul Zarek	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/31/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 3, 5, 6, and 12-14 have been amended by the Applicant in correspondence filed on 08/31/2009. Claims 1-14 are currently pending. This is the second Office Action on the merits of the claim(s).

RESPONSE TO ARGUMENTS

2. Examiner acknowledges the amendments to the instant specification filed on 08/31/2009. Through these amendments, Applicant has perfected the claim to the prior-filed international application no. PCT/US04/19812 (filed on 06/21/2004), which claims the benefit of prior-filed provisional application no. 60/480,206, filed on 06/20/2003. The effective filing date of the instant application is 06/20/2003. Furthermore, the objection to the disclosure is moot in light of these amendments.

3. Claims 5-7 and 12-14 were objected to for various typographical errors. These objections are moot in light of Applicant's amendment to Claims 5-7 and 12-14.

4. Claims 1-14 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. Applicant traversed this rejection on the grounds that Examiner's conclusion of a lack of enablement is incorrect in light of a careful reading of the specification. Specifically, Applicant asserts that the results and conclusions declared in Ostrow, et al. (Antiviral Research, 1994), are based on work done on cottontail rabbit papilloma virus, which Applicant alleges is a poor paradigm for human papilloma viruses (HPVs). Thus, Applicant

asserts that Ostrow, et al., is not relevant to the findings of the present inventor. Applicant believes Examiner's suggestion that CTC-96 (also known as Doxovir™) is ineffective to treat papilloma virus is wrong, in light of both the instant specification and the prior art.

5. Applicant directs Examiner's attention to the median values of graft size as disclosed in Table 5. Applicant mentioned that Examiner "used only means of graft size without the standard deviation which is reflected in the median values."

6. Applicant points to *ex vivo* data (Tables 3, 4, 6, and 7) demonstrating that CTC-96 reduced the number of HPV-positive grafts in a dose-dependent fashion. Applicant also provides Exhibit A which allegedly shows the effectiveness of CTC-96 on graft size, and asserts that Exhibit A shows "a dramatic and distinct statistically significant microbicidal effect of CTC 96." Applicant indicated this exhibit would be submitted with a declaration by the inventor. Examiner notes that no such declaration is on file.

7. Respectfully, Examiner does not find Applicant's arguments persuasive.

8. Examiner acknowledges that CTC-96 blocks bovine papilloma virus (BPV) from transforming cells, *in vitro*, and removes or reduces HPV in foreskin grafts on SCID mice. However, the claims are drawn to a method of therapeutic treatment of a disease in a subject caused by papilloma virus comprising administration of CTC-96 to the subject. Reducing or removing papilloma virus from a subject is <u>not</u> the same as treating a disease caused by papilloma virus (i.e. papilloma virus-induced tumor). Thus, the data shown in Tables 2-4, and 6-11 do not, by themselves, demonstrate that CTC-96 is efficacious at treating or avoiding a disease caused by papilloma virus.

9. Tables 1 and 5 in the instant disclosure indicate that CTC-96 has no effect on graft growth. In Table 1, the result of the control (2.58 ±0.808 mm) encompasses the entirety of the experimental samples. The specification interprets the results in Table 1 to indicate that "there was a small but significant effect on the infectivity of HPV-11 when compared to the control" (pg 6, para 0023, emphasis added). There is no interpretation of Table 1 with respect to the effect of CTC-96 on graft size. In this model, the growth of the graft is the disease caused by papilloma virus. While Table 1 shows that the median graft size is smaller in the experimental groups relative to the control group and that graft size reduction appears to be in a dose-dependent fashion, the small sample size (n=9) of the control would not allow an art worker to discard the outlier(s) as anomalies to be removed from interpreting the data.

10. Table 5 suffers from a similar deficit. The graft grows 57.50 ±48.59% in the control group, and the presence of 0.1% or 1% CTC-96 has no effect on graft size (graft grows 64.53 ±41.92% or 91.39 ±127.84%, respectively). The median graft growth for the three conditions was similar, (50.65% (control), 60.51% (0.1% CTC-96), and 52.03% (1% CTC-96)). The interpretation disclosed in the instant specification states that "[t]he ANOVA fails to show a treatment effect on the growth of individual grafts" (pg 10, para 0032).

11. Examiner notes that Exhibit A has been submitted without the support of a declaration. As such, it will be accorded the weight of an argument, only. The data contained within Exhibit A does not persuasively demonstrate that the reduction in graft size is caused by administration of CTC-96. Likewise Table 1, the standard deviation of the control group is sufficiently large that it masks any effects that CTC-96 may have on tumor size. Furthermore, Figure 1 of the provisional '206 application shows no difference on the percentage of graft growth in control and

CTC-96-treated SCID mice. Taken together, the data disclosed in Tables 1 and 5 of the instant specification, Exhibit A, and Figures 1 and 2 of the provisional application indicate that CTC-96 has no effect on HPV-induced graft growth, *in vivo*.

12. The findings of the instant specification are consistent with those disclosed in the prior art. Ostrow, et al., found that rabbits treated with CTC-96 displayed a dose-dependent increase in tumor size, time to first tumor, and number of rabbits developing tumor (Table 1). The tumor is interpreted to be a disease caused by papilloma virus. The differences were statistically significant with $P<0.001$ for tumor size. Ostrow, et al., state that their results "show that the use of [CTC-96] may be contraindicated in patients with papillomavirus infections" (pg 29, lines 9-10, emphasis added). Applicant's argument that cottontail rabbit papilloma virus is a poor paradigm for HPV or BPV is not persuasive for two reasons: 1) there is no limitation in the claims that the disease to be treated has to be caused by HPV or BPV; and, 2) Applicant has provided no evidence why cottontail rabbit papilloma virus is a "poor paradigm" for other papilloma viruses.

13. Bonnez, et al. (Proceedings of the 18th International Papilloma Conference, 2001, provided in IDS), disclose that CTC-96 (termed Doxovir™) "had no proliferative or inhibitory effect on the growth of HPV-11-infected human grafts." Thus, the data of Bonnez, et al., corroborates the disclosure of the instant specification and the teachings of Ostrow, et al.

14. For the above reasons, the rejection of Claims 1-14 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is maintained.

15. Claims 1-14 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as

the invention. The rejected claims are drawn to a method comprising administration of "an anti-papilloma virus disease effective amount of CTC-96." This rejection is withdrawn in light of Applicant's arguments.

16. Claims 1-14 are examined on their merits and the following **FINAL** rejection is made based on art that was provided in an IDS filed after the First Action on the Merits.

Conclusion

17. Claims 1-14 remain rejected.

18. Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on *08/31/2009 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul Zarek whose telephone number is (571) 270-5754. The examiner can normally be reached on Monday-Thursday, 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

PEZ

/San-ming Hui/
Primary Examiner, Art Unit 1628